Attorney's Docket No.: 21865-002001 / 6502 Applicant: Yu et al. Preliminary Amendment and RCE

Serial No.: 10/718,986

: November 21, 2003

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions and listings of claims in the application.

LISTING OF CLAIMS:

(Currently amended) A protein based composition, comprising a compound that 1. comprises:

at least one therapeutic domain comprising a peptide or protein, wherein the at least one therapeutic domain has at least one extracellular enzyme or enzyme inhibitor sialidase activity that can prevent the infection of a target cell by a pathogen by blocking entry into the target cell; and

at least one anchoring domain comprising a peptide or protein, wherein the anchoring domain binds to a glycosaminoglycan (GAG) can bind to a molecule on the surface of the target cell.

- (Currently amended) The composition compound of claim 1, wherein the target cell is 2. an epithelial cell or endothelial cell and the anchoring domain can bind to a molecule on the surface of the epithelial or endothelial cell.
- (Currently amended) The composition compound of claim 2, wherein the target cell is 3. an epithelial cell and the anchoring domain can bind to a molecule on the surface of the epithelial cell.
- (Canceled) 4.
- (Canceled) 5.
- (Currently amended) The composition compound of claim [[5]] 3, wherein the 6. anchoring domain can bind heparin or heparan sulfate.
- (Currently amended) The composition compound of claim 6, wherein the anchoring 7. domain is a peptide.

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8. (Currently amended) The composition compound of claim 7, wherein the peptide comprises a GAG-binding amino acid sequence of a naturally-occurring protein, or a sequence that is substantially homologous to the GAG binding sequence of a naturally-occurring protein.

- 9. (Currently amended) The composition compound of claim 8, wherein the peptide comprises the GAG-binding amino acid sequence of a mammalian protein.
- 10. (Currently amended) The composition compound of claim 9, wherein the peptide comprises the GAG-binding amino acid sequence of a human protein.
- 11. (Canceled)
- 12. (Currently amended) The eomposition compound of claim 10, wherein the amino acid sequence comprises the GAG-binding amino acid sequence of human platelet factor 4 (SEQ ID NO:2), human interleukin 8 (SEQ ID NO:3), human antithrombin III (SEQ ID NO:4), human apoprotein E (SEQ ID NO:5), human angio-associated migratory protein (SEQ ID NO:6), or human amphiregulin (SEQ ID NO:7), or a sequence that is substantially homologous thereto.
- 13. (Currently amended) The composition compound of claim 1, wherein the pathogen is a virus.
- 14. (Currently amended) The composition compound of claim 13, wherein the virus is an influenza virus.
- 15-21. (Canceled)
- 22. (Currently amended) The <u>composition compound</u> of claim 1, wherein the therapeutic domain is <u>a sialidase</u> an enzyme or an active portion thereof, wherein the active portion retains enzymatic activity and does not comprise the full length enzyme.

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23. (Canceled)

24. (Currently amended) The composition compound of claim [[23]] 22, wherein the sialidase is or is substantially homologous to at least one viral sialidase, at least one bacterial

sialidase, or at least one eukaryotic sialidase.

25-30. (Canceled)

31. (Currently amended) The composition compound of claim 24, wherein the sialidase

is or is substantially homologous to at least one eukaryotic sialidase.

32. (Currently amended) The composition compound of claim 31, wherein the sialidase

is or is substantially homologous to at least one human sialidase.

33. (Currently amended) The composition compound of claim 32, wherein the human

sialidase is or is substantially homologous to the NEU1, NEU3, NEU2, or NEU4 genes.

34. (Currently amended) The composition compound of claim 33, wherein the sialidase

is or is substantially homologous to the NEU2 or NEU4 genes and comprises a sequence of

amino acids that is or is substantially homologous to the sequence of amino acids set forth in

SEQ ID NO:8 or SEQ ID NO:9.

35-46. (Canceled)

47. (Currently amended) A pharmaceutical formulation comprising the composition

compound of claim 1.

48-49. (Canceled)

50. (Withdrawn) A method for the prevention, prophylaxis or treatment of influenza

infection, comprising: applying a therapeutically effective amount of the composition of

claim 1 to target cells of a subject.

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51-53. (Canceled)

54. (Withdrawn) A method of using a sialidase for the prevention, prophylaxis or

treatment of infection by a pathogen, comprising:

applying a therapeutically effective amount of the composition of claim 23 to target

cells of a subject.

55. (Withdrawn) The method of claim 54, wherein the sialidase is or is substantially

homologous to at least one viral sialidase, at least one bacterial sialidase, or at least one

eukaryotic sialidase.

56. (Withdrawn) The method of claim 55, wherein the sialidase is or is substantially

homologous to at least one eukaryotic sialidase.

57. (Withdrawn) The method of claim 56, wherein the subject is a human subject and

the sialidase is or is substantially homologous to at least one human sialidase.

58. (Withdrawn) The method of claim 57, wherein the sialidase is or is substantially

homologous to the NEU2 or NEU4 genes and comprises a sequence of amino acids that is or

is substantially homologous to the sequence of amino acids set forth in SEQ ID NO:8 or SEQ

ID NO:9.

59-60. (Canceled)

61. (Currently amended) The composition compound of claim 24, wherein the sialidase

is or is substantially homologous to at least one bacterial sialidase.

62. (Currently amended) The composition compound of claim 61, wherein the bacterial

sialidase is selected from the group consisting of Vibrio cholerae sialidase, Clostridium

perfringens sialidase, Actinomyces viscosus sialidase and Micromonospora viridifaciens

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sialidase.

63. (Currently amended) The composition compound of claim 61, comprising only one bacterial sialidase.

64. (Currently amended) The composition compound of claim 63, wherein the bacterial sialidase is *Actinomyces viscosus* sialidase.

65. (Currently amended) The composition compound of claim 1, further comprising at least one peptide linker that links the anchoring domain to the therapeutic domain.

- 66. (Currently amended) The composition compound of claim 65, wherein the peptide linker comprises at least one glycine residue.
- 67. (Currently amended) The composition compound of claim 65, wherein the peptide linker comprises the sequence (GGGGS)n, where n is a whole number from 1 to 20.
- 68. (Currently amended) The eomposition compound of claim 1, wherein the anchoring domain is N-terminal to a therapeutic domain.
- 69. (Currently amended) The <u>composition compound</u> of claim 1, wherein the anchoring domain is C-terminal to a therapeutic domain.
- 70. (Currently amended) The composition compound of claim 1, comprising at least two anchoring domains.
- 71. (Currently amended) The <u>composition compound</u> of claim 70, wherein at least one of the anchoring domains is N-terminal to a therapeutic domain and at least one of the anchoring domains is C-terminal to a therapeutic domain.
- 72. (Previously presented) The pharmaceutical formulation of claim 47 that is formulated as a spray.

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73. (Previously presented) The pharmaceutical formulation of claim 47 that is formulated as an inhalant.

74. (Currently amended) The composition compound of claim 3, wherein the epithelial cell is a respiratory epithelial cell, an adenoid epithelial cell or a bronchial epithelial cell.

- 75. (Currently amended) The composition compound of claim 13, wherein the virus is selected from among parainfluenza and respiratory syncytial virus
- 76. (Previously presented) The pharmaceutical formulation of claim 47 that is formulated as a suspension, a solution for injection or a solution for oral administration.
- 77. (Previously presented) The pharmaceutical formulation of claim 47 that is formulated as a solution for eye drops.
- 78. (Previously presented) The pharmaceutical formulation of claim 47 that is formulated as a cream, salve, gel, or ointment.
- 79. (Previously presented) The pharmaceutical formulation of claim 47 that is formulated as a tablet, capsule or lozenge.
- 80. (Currently amended) A delivery system, comprising the pharmaceutical formulation of claim 72 or claim 73 and a device selected from among a nebulizer, an atomizer and a dropper bottle.
- 81. (Canceled)
- 82. (Withdrawn) The method of claim 55, wherein the sialidase is or is substantially homologous to at least one bacterial sialidase.

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83. (Withdrawn) The method of claim 82, wherein the bacterial sialidase is selected from the group consisting of *Vibrio cholerae* sialidase, *Clostridium perfringens* sialidase, *Actinomyces viscosus* sialidase and *Micromonospora viridifaciens* sialidase.

- 84. (Withdrawn) The method of claim 83, wherein the bacterial sialidase is *Actinomyces viscosus* sialidase.
- 85. (Withdrawn) The method of claim 54, wherein the applying is by use of a nasal spray.
- 86. (Withdrawn) The method of claim 54, wherein the applying is by use of an inhaler.
- 87. (Withdrawn) The method of claim 54, wherein the applying is by oral administration.
- 88. (Withdrawn) The method of claim 54, wherein the applying is performed from once to four times a day.
- 89. (Withdrawn) The method of claim 54, wherein the pathogen is a bacterium.
- 90. (Withdrawn) The method of claim 54, wherein the pathogen is a virus.
- 91. (Withdrawn) The method of claim 90, wherein the virus is selected from among influenza, parainfluenza and respiratory syncytial virus.
- 92. (Withdrawn) The method of claim 91, wherein the virus is influenza virus.
- 93. (Withdrawn) The method of claim 54, wherein the subject is a human subject or an animal subject.
- 94. (Currently amended) The composition compound of claim 12, wherein the therapeutic domain is or is substantially homologous to:
 - a human sialidase selected from among the NEU1, NEU3, NEU2, or NEU4 genes; or

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a bacterial sialidase selected from among Vibrio cholerae sialidase, Clostridium perfringens sialidase, Actinomyces viscosus sialidase and Micromonospora viridifaciens

sialidase.

95. (Currently amended) The composition compound of claim 1, comprising an additional domain selected from among proteins, peptides, carbohydrates, fatty acids, lipids, steroids, nucleotides, nucleotide analogues, nucleic acid molecules, nucleic acid analogues,

peptide nucleic acid molecules, organic molecules, and polymers.

96. (Currently amended) The composition compound of claim 95, wherein the additional

domain is a purification domain, a domain that improves the solubility or distribution of the

compound, a linking domain, a stability-conferring domain, a domain that contributes to the

three dimensional structure of the compound, or a domain that increases the size of the

compound.

97. (Currently amended) The composition compound of claim 96, wherein the domain is

a linking domain that links the therapeutic and anchoring domains.

98. (Currently amended) The composition compound of claim 96, wherein the domain is

a linking domain that links chemical moieties to the compound.

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